The role of biology today, like the role of every other science, is simply to describe, and when it explains it does not mean that it arrives at finality; it only means that some descriptions are so charged with significance that they expose the relationship of cause and effect.
Donald Culross Peattie (1898–1964)

CHEMICAL EXPOSURES

Prostate Cancer and Early BPA Exposure

In animal models, estrogens can drive carcinogenesis of the prostate and have long been suspected of playing a role in human prostate cancer. Scientists have hypothesized that prenatal exposure to estrogen-like compounds, including monomeric bisphenol A (BPA), may account for recent increases in rates of prostate cancer. Now a rat study by Gail Prins of the University of Illinois at Chicago Department of Urology, Shuk-Mei Ho of the University of Cincinnati Department of Environmental Health, and their colleagues provides the first evidence of a direct link between low-dose BPA exposure during development and later prostate cancer.

BPA initially was synthesized for use in estrogenic-type drugs. BPA also is used as a cross-linking compound in the manufacture of polycarbonate plastics and epoxy resins. It leaches from food and beverage containers and from dental sealants, although the latter currently are not thought to be a major source of exposure. Today, this hormonally active chemical is widespread in the environment, with detectable serum levels present in approximately 90% of humans in the United States and other industrialized countries, by Prins's estimate. BPA concentrations measured in placental and fetal tissues may be fivefold higher than maternal serum levels, with higher levels found in male fetuses compared to females, according to Prins.

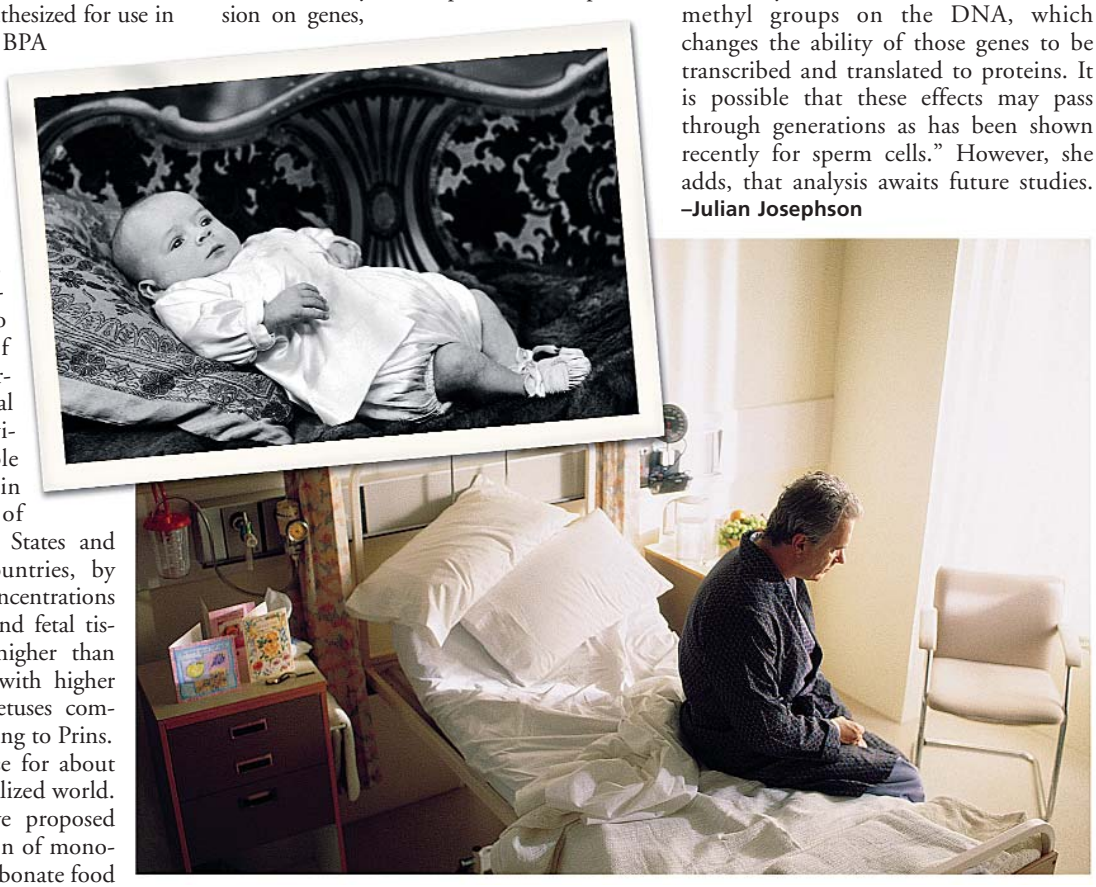
BPA has been in use for about 50 years in the industrialized world. Some investigators have proposed that widespread ingestion of monomeric BPA from polycarbonate food and drink containers might partially explain recent increases in prostate cancer rates. According to the American Cancer Society, rates have been on the rise since 1975. With the 1987 introduction of prostate-specific antigen testing, the newly enhanced ability to diagnose the disease caused incidence to spike to 240 age-adjusted cases per 100,000 men by 1992. After this "catch-up" period, rates dropped for three years, but are now back on the rise.

In the study, described in the 1 June 2006 issue of *Cancer Research,* groups of newborn rats were given high or low doses of estradiol or an environmentally relevant dose of BPA. The findings provide a molecular underpinning for potential long-term effects by showing changes in methyl groups on DNA that are responsible for turning genes on or off. For example, one key prostate gene that normally fuels cell growth during development stayed turned on in the prostates of male rats exposed to BPA or elevated estradiol from birth, says Prins. Such epigenetic alterations may leave a permanent impression on genes, possibly sensitizing the animal to developing diseases later in life.

One must exercise caution, however, in extrapolating the current rat findings to humans. How might one conduct an analogous program of research on men? The researchers consider such a program virtually impossible because 50 years or more typically would be required for results of early exposure to BPA to show up as prostate cancer.

Indeed, Rebecca Sokol, a professor of medicine at the University of Southern California, cautions against extrapolating human effects from rat studies. She does, however, note that unlike strong carcinogens that damage DNA profoundly, BPA appears to cause subtle changes that may pass from one generation to the next. She asks whether something is happening to alter genes seemingly without changing the genetic code itself.

Says Prins, "Our evidence shows that in an animal model, some genes are altered by the addition or removal of methyl groups on the DNA, which changes the ability of those genes to be transcribed and translated to proteins. It is possible that these effects may pass through generations as has been shown recently for sperm cells." However, she adds, that analysis awaits future studies.
–Julian Josephson



Disease through the ages. New rat data link BPA exposure during critical periods of early development to later prostate cancer, raising compelling questions for research in humans.

Digital Vision; inset: Eclectic Collections

Policy

WHO/ILSI Affiliation Sustained

The International Life Sciences Institute (ILSI) is set to be honored for its Physical Activity and Nutrition program as part of the September 2006 National Congress on Accelerating Improvement in Childhood Obesity in Washington, DC. The program is being singled out for its innovative approaches to educating children, parents, and caregivers about managing child obesity. However, such praise contrasts sharply with criticism that was leveled at ILSI just months ago.

At a 27 January 2006 meeting in Geneva, the WHO Executive Board reviewed ILSI's NGO status, along with that of several other NGOs, as part of the WHO's standard three-year review cycle. The National Resources Defense Council, an environmental action group, was calling for the WHO to sever its relationship with ILSI, based on the fact that ILSI's membership includes representatives of major multinational corporations with a vested interest in public health matters.

The board ultimately decided to maintain official relations with ILSI, describing its role as "a knowledge resource base for the application of leading-edge science and knowledge transfer in the fields of food and chemical safety." ILSI is therefore still permitted to attend WHO governing body meetings and make statements at these meetings. Although this presence does not come with voting privileges, it affords such an organization valuable "insider" status. However, this latest decision by the Executive Board does exclude any collaboration by ILSI on normative activities, defined as "setting microbiological or chemical standards for food and water."

According to Harvey Anderson, who chairs ILSI's Board of Trustees, the organization has never taken part in such activities anyway. While its strongest critics accuse ILSI of working behind the scenes to present information that would shape public policy to corporate advantage, Anderson points out that ILSI functions according to a nonprofit charter bound by U.S. regulations, with a board dominated by members not affiliated with any vested interest, who would readily vote down such lobbying.

"ILSI is overrun by lawyers making damn sure everybody holds to the charter," he explains, noting that representatives like himself—a nutritional sciences professor at the University of Toronto—are unpaid volunteers devoting a great deal of time and energy to what they regard as a research endeavour.

"ILSI has gathered some of the top scientists from around the world to work with industry and work with government and work with their colleagues on issues that need this kind of cooperative approach," says Anderson. "We publish our research and reports in journals that require peer review by their standards and by scientists of their choice."

Observers such as Jennifer Sass, a scientist with the Natural Resources Defense Council, insist that this approach nevertheless yields skewed science. Her group drafted a letter of protest that was circulated by hand at the Geneva meeting, citing examples of ILSI's undue influence in shaping the conclusions of scientific studies on issues such as the role of sugar in diet and the designation of cancer-causing agents.

"Their documents come out in one direction, which is always somewhere between 'everything's okay' and 'we need more study,'" she says, referring to ILSI's participation in a 1998 study that denied finding evidence of a direct link between sugar intake and lifestyle-related diseases. According to Sass, that conclusion conflicts with the results from a 1990 WHO study group, which recommended health policy targets that reflect the increased risks of chronic diseases caused by dietary patterns that include high sugar intake.

"They never come out as 'this is a big problem and we should do something about it,'" says Sass, adding that governments can perpetuate a misrepresentation of this research by condoning ILSI's approach.

Similar complaints voiced in the 1990s were followed by a 2001 report by the WHO Tobacco-Free Initiative on how member tobacco companies had used ILSI to muster seemingly unbiased scientific opinions aimed at quashing WHO tobacco control efforts. ILSI vehemently denied these allegations and, Anderson says, worked with the WHO to provide assurances of transparency about how ILSI operates.

Derek Yach, now head of the Rockefeller Foundation's Program on Global Health, led that WHO initiative and closely watched ILSI's response. "Part of the problem lies with the UN agencies themselves, or in this case the WHO," he concludes, noting that these bodies have yet to take many of the protective measures recommended by the report. "You can blame the corporations," he says, "but you also need to place blame on not having very clear, very transparent review of conflict-of-interest procedures internally." **–Tim Lougheed**

Top to bottom: AP Photo/*Daily Post-Athenian*, Ben Benton; AP Photo/Ben Curtis

Tracking Toxicants in Canadians

Health Canada announced in May 2006 that it would begin a national biomonitoring program to measure levels of toxic chemicals in the bodies of Canadians. The announcement came as the NGO Environmental Defense prepared to release the results of its own tests, the first look at the amounts of chemicals showing up in Canadian adults and children. That study found 46 of 68 chemicals tested for, with an average of 32 chemicals appearing in adults and 23 in children. Compounds such as polychlorinated biphenyls and DDT were found in children born years after these chemicals were banned. It is not yet known whether the new program, set to begin in late 2007, will be permanent.

Citizens Want Free Access to Research Findings

The results of an online Harris poll released 1 June 2006 show that 82% of U.S. adults believe the findings of federally funded research should be available for free online, and that 62% believe free access would lead to quicker discoveries that positively impact health. Heather Joseph, executive director of the Scholarly Publishing and Academic Resources Coalition, commented, "The public recognizes its stake in open sharing of resources, and the Harris data gives voice to their stand." Senators John Cornyn (R–Texas) and Joseph Lieberman (D–Connecticut) recently introduced the Federal Research Public Access Act of 2006, which would require federal agencies that fund over $100 million in external research per year to make their study results publicly available online.

Roadside Meth Risk

According to the National Advisory Council on Drug Abuse, every pound of methamphetamine produced means 5 to 7 pounds of toxic materials. Now roadside cleanup volunteers and maintenance workers are being educated about the dangers of picking up litter tossed out when meth labs clean house. People coming across such materials can experience skin burns or lung damage from touching or inhaling fumes from meth waste. Several state and local agencies have created brochures and videos to educate their workers. Hints indicating a roadside meth dump site include bottles with rubber hoses attached, the smell of ammonia, and coffee filters stained red or containing a white powdery residue.

INFECTIOUS DISEASE

A Deadly MIF

Up to 2 million children die each year from malaria, with about half dying from malaria-induced anemia. Scientists aren't sure why some malaria patients develop this life-threatening complication and others don't. A study published in the 15 May 2006 *Journal of Experimental Medicine* suggests the blame rests in part on macrophage migration inhibitory factor (MIF), an immune cytokine produced by white blood cells.

Unraveling a life-threatening complication. A genotyping project at Macha Mission Hospital in Zambia, where director Phil Thuma (center) conducts pediatric rounds, aims to prevent malaria-induced anemia in children.

The paper's authors suspected that MIF might suppress bone marrow activity, because polymorphisms of the *MIF* gene increase susceptibility to different inflammatory and infectious disorders. "MIF appears to be part of an over-exuberant response on the part of the immune system in a number of diseases, so it was a logical choice for us to look at," says coauthor Michael A. McDevitt, a hematologist at the Johns Hopkins University School of Medicine. The team infected mice that were genetically modified to lack the *Mif* gene with malaria parasites. About one-third of those mice survived, compared to only 9% of the normal mice.

MIF doesn't act alone, the researchers discovered when they took progenitor cells from the bone marrow of mice and allowed the cells to grow both with and without MIF and two other immune factors, TNFα and IFNγ. Applied alone in low concentrations, none of the immune factors seriously damaged the bone marrow cells. "But when we added all three together at the same low levels, we witnessed a synergistic poisoning of bone marrow," says McDevitt.

MIF probably prevents cells in the bone marrow from responding to erythropoietin, the hormone that triggers red blood cell production, says coauthor Richard Bucala, an immunologist and rheumatologist at Yale University School of Medicine. Some people's immune system may make too much MIF in response to malarial infection. About 30% of the population in Africa, where malaria is rampant, produces excessive MIF protein, earlier studies have shown.

MIF isn't the only cause of malarial anemia. The *Plasmodium* parasite destroys red blood cells, and the spleen also removes infected and even some uninfected cells. "The pathogenesis of [malarial] anemia has been a mystery for a long time," says Peter J. Hotez, a parasitologist at George Wash*ington University. "This mouse* study adds to the evidence . . . that MIF impedes the production of red blood cells."

Understanding the mechanisms behind malarial anemia could help direct future therapies. MIF is the key therapeutic target, because blocking it alone protects the cells, whereas blocking TNFα or IFNγ alone doesn't, explains Bucala. Since the blood transfusions needed to treat severe anemia are often difficult for many poor families to find or afford, researchers hope to determine early on which children need immediate care to prevent the anemia.

To that end, Bucala and colleagues are collaborating on a project with Macha Mission Hospital in Zambia to assess the frequency of *MIF* polymorphisms in children with malarial anemia. They use a new, inexpensive method to identify the polymorphism in just 2 hours, letting them know whether a child will likely need a transfusion. In Zambia, children have a well-baby visit soon after birth, and it is possible every baby could get genotyped, says Bucala, who adds, "Then the mother would know that if her child develops fever in the rainy season, she should go to the hospital quickly." **–Tina Adler**

ENVIRONMENTAL DISEASE

Ozone: Good, Bad, or Indifferent?

Following up on their eye-catching finding that the human body generates its own ozone for beneficial purposes, a team of U.S. and British researchers now describe specific processes through which ozone can react with cholesterol and contribute to atherosclerosis, or hardening of the arteries. Whether the ozone involved comes from within the body or from the environment remains unclear, however, and the team's findings remain controversial on several counts.

In earlier work, Paul Wentworth, Jr., a chemistry professor at The Scripps Research Institute, and colleagues concluded that self-generated ozone is used by the immune system's antibodies and neutrophils to destroy bacteria and fungi. They published a study in 2003 showing that ozone can damage the vascular system by contributing to atherosclerosis. They also noted the same process may play a role in diseases such as lupus, multiple sclerosis, and rheumatoid arthritis.

The mechanism by which such damage occurs wasn't clear in the 2003 study, however. Some of that information was filled in with a report published 13 June 2006 in *Biochemistry*. Through a series of *in vitro* tests, the team exposed human and mouse cells to two by-products of ozone's interaction with cholesterol, atheronal-A and atheronal-B. They found that one, the other, or both atheronals accelerate the normal conversion of monocytes to macrophages, are rapidly taken up by macrophages, hasten the inflammatory response on and increase the stickiness of the interior arterial walls, and contribute to the formation of arterial plaques.

Numerous questions remain about the research protocols (such as a lack of controls to prove that ozone was the oxidant at work) and conclusions regarding the body's self-generation of ozone (such as whether cells are likely to expend so much energy to produce their own ozone), says William Pryor, director of the Biodynamics Institute at Louisiana State University. Further, there is little solid evidence that environmental ozone plays a role in this specific process, although exposure to atmospheric ozone has been implicated in a number of cardiovascular problems, including heart attack and changes in heart rhythm.

Wentworth acknowledges that increased cholesterol ingestion may be the most important driving factor in the atherosclerotic damage his team found—many of the harmful atheronal processes occurred only when "bad" LDL cholesterol was present. Still, this line of inquiry may contribute to better insights about the complex relationships between the body's normal functions, reactive oxygen species including ozone, and cardiovascular damage, leading even its critics to say this concept deserves attention, analysis, and more research. **–Bob Weinhold**

Rick Bucala/Yale University

ehpnet

Collaborative on Health and the Environment Toxicant and Disease Database

From huge industrial spills to exposure to everyday products, there are a number of ways people come in contact with potentially hazardous chemicals. To help educate those wanting more in-depth information about the health effects of chemicals, the Collaborative on Health and the Environment (CHE) has developed the CHE Toxicant and Disease Database, available online at http://database.healthandenvironment.org/.

The CHE was formed in 2002 as a project of the nonprofit health and environmental research institute Commonweal with a mission to foster a greater understanding of the links between human health and the environment. The database, which summarizes links between chemical contaminants and approximately 180 human diseases and conditions, has been enhanced recently with new search features and a directory of links to other resources that would be of interest to visitors to the CHE site.

Background information on the theory behind the database project is available through a link in the text paragraph near the top of the homepage. Here, visitors can learn about the nature of gene–environment interactions and their impacts on human health; the lack of toxicity data on many of the 80,000-plus chemicals that have been developed, distributed, and discarded over the past 50 years; and the difficulties encountered in assessing the risk of chemical exposures. This page also describes where the information in the database came from, how chemicals are categorized, and what limitations there are to the database.

The homepage features an alphabetical listing of diseases and conditions—ranging from abnormal sperm to Wilm's tumor—that can potentially be triggered by exposure to environmental chemicals. Each disease or condition links to a page listing its chemically related causes. These causes are grouped by the strength of evidence—strong, good, or limited—of the relationship between the health effect and the chemical. Each page also cites references. Choosing one of the listed chemical causes brings up a record of all of the diseases and conditions linked to that chemical.

The database can be searched using one of the pull-down lists at the right of the homepage. There are options for searching by any of 25 disease categories, by individual disease, or by any of dozens of toxicants. Searches can also be performed by Chemical Abstract Service number and by keyword.

The directory available through the Links to Other Databases and Resources link cites 17 databases, including ones hosted by the NIEHS, the CDC, the EPA, the ATSDR, and the International Agency for Research on Cancer. Other resources listed include the CDC's *National Report on Human Exposure to Environmental Chemicals*, the National Toxicology Program and its *11th Report on Carcinogens*, the California Office of Environmental Health Hazard Assessment, and *EHP*. **–Erin E. Dooley**

Cairo Hails New Fleet of Eco-Cabs

Cairo is known for its poor air quality, with its near-permanent haze a mix of industrial emissions, desert sand, and car exhaust fumes. In March 2006, a small fleet of new taxis hit the streets of Egypt's capital city. Unlike their predecessors, the 150 new yellow Hyundais and Volkswagens feature catalytic converters to filter their exhaust, along with air conditioning and seat belts. A scheme laid out by Egyptian prime minister Ahmed Nazif calls for a total of 1,500 new taxis to be available by the end of 2006. *The Christian Science Monitor* reported on 1 June 2006 that the Egyptian government is also considering fueling the vehicles with natural gas.

Living Low Poses Risk

Although only 2.2% of the world's land area is less than 10 meters above sea level, 10% of the world's population—some 600 million people—lives at these low elevations. Of these, 60% live in urban areas. A report in the April 2006 news bulletin *Tiempo* by researchers from The Earth Institute at Columbia University states these people are at risk from rising sea levels and increasingly strong storms due to climate change. Geographical location isn't the only factor that determines vulnerability, however. Although the United States has more urban areas in low-elevation coastal zones than any other country, low-income countries and those designated as Least Developed Countries have fewer resources to rebound from the effects of climate variability.

A Plan for Farm Plastics

Farmers use "ag plastics" for a wide variety of purposes—dairy and silage bags, coverings for crops, wrappings for hay bales, and more—and thousands of tons are burned, buried, or dumped annually. Now Cornell University researcher Lois Levitan is developing a pilot program to collect and recycle used plastic film sheeting from New York dairies and nurseries.

Levitan reports that about half of discarded ag plastic is burned, which generates emissions of dioxin and other hazardous chemicals. Other waste plastic is often plowed into the ground, where it can become a breeding place for insect pests as well as trap and choke wildlife. Levitan suggests recycling plastics into fence posts, plastic lumber, garbage bags, and other uses, or converting the plastic resin content to a fuel.

Top to bottom: Art Explosion; CHE; Patricia Marroquin/Shutterstock